Primary Leiomyosarcoma in the Inferior Vena Cava Extended to the Right Atrium: A Case Report and Review of the Literature

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Keywords
Leiomyosarcoma · Inferior vena cava · Right atrium

Abstract
A 38-year-old woman had developed an abdominal distention, lower extremity edema, and dyspnea. Imaging examination revealed a large mass in the right atrium which was connected to lesions within the inferior vena cava. Although complete resection of the mass was not possible, partial surgical tumor resection was performed to avoid pulmonary embolization and circulatory collapse. Leiomyosarcoma was diagnosed histologically, and chemotherapy (doxorubicin) followed by radiotherapy was started. By reviewing papers published in the past 10 years that included 322 patients, we also discuss the clinical presentations and prognosis of leiomyosarcoma in the inferior vena cava.
**Introduction**

Leiomyosarcoma is a rare, malignant mesenchymal tumor; only 218 cases had been reported as of 1996 [1]. Leiomyosarcoma of vascular origin often occurs in the inferior vena cava, and one that originated from the wall of the inferior vena cava was first reported by Perl [2] in 1871. In a previous study, it was found that patients with inferior vena cava involvement may present with lower extremity edema; however, symptoms may be nonspecific, and overall prognosis is reported to be poor, with a median survival of 2 years [3].

We herein report the case of a 38-year-old woman with primary leiomyosarcoma that was thought to originate from the inferior vena cava and to extend to the cardiac cavity. We also review case reports describing primary intimal sarcomas of the inferior vena cava from the past 10 years, and discuss the prevalence of symptoms and compare survival periods in this relatively recent literature.

**Case Report**

A 38-year-old female patient experienced abdominal distension, lower extremity edema, and dyspnea from January 20xx. Elevation of hepatic enzyme levels, ascites, and enlargement of the inferior vena cava were found, and therefore the patient was admitted to her former hospital. Further examinations revealed a mass in the right atrium which extended to the inferior vena cava and hepatic and renal veins; thus, she was referred to our department for further diagnosis and treatment.

On admission, her vital signs showed a blood pressure of 138/96 mm Hg and a heart rate of 92 beats/min. Her abdomen was round and edema was present in both of the lower extremities. Chest X-ray revealed a normal cardiothoracic ratio of 48%. Electrocardiography did not show any apparent abnormal findings (fig. 1); it showed a preserved left ventricular ejection fraction of 61% and a tumor 33.0 × 35.7 mm in size in the right atrium that continued to the cavity of the inferior vena cava.

Laboratory studies showed a white blood cell count of 11,550 cells/µl, a hemoglobin level of 14.3 g/dl, a platelet count of 32.0 × 10^4 cells/µl, and a D-dimer level of 5.7 μg/ml. Alanine transaminase and aspartate transaminase levels were elevated to 464 and 509 U/l, respectively. The levels of carcinoembryonic antigen, α-fetoprotein, CA19-9, and CYFRA 21-1 were within normal limits, but those of CA125 (389.9 U/ml) and PIVKA-II (43 mAU/ml) were elevated.

Computed tomography and magnetic resonance imaging showed dilatation of the inferior vena cava and tumor occupation between the right atrium and the inferior vena cava (fig. 2a–d), ascites, and myoma of the uterus. Subsequent 18F-FDG-PET (18F-fluorodeoxyglucose positron emission tomography) showed increased nuclear uptake only in the mass in the right atrium (fig. 2e, f). Coronary angiograms showed no apparent coronary artery stenosis, with small arteries feeding the tumorous lesion from the right coronary artery and the left circumflex artery (data not shown).

Although complete resection of the tumor was considered to be difficult, a surgical approach was taken for the purpose of amelioration of hepatic congestion and avoidance of circulatory shock. The heart was exposed through a median sternotomy, and a cardiopulmonary bypass was established with an ascending aortic arterial return and venous drainage through the cannulae, one placed in the superior vena cava and the other directly into the right atrium via the appendage. The systemic temperature was reduced to 24°C, after which
the circulation was interrupted and the venous blood drained into an oxygenator. The right atrium was opened down to the inferior vena caval orifice. The intra-atrial portion of the solid tumor was carefully dissected, so as to prevent embolization, and then excised. The tumor was fragmented and removed by applying hundreds of bites with pituitary rongeurs so that the caval junctions of all the hepatic veins could be fully recanalized. After full rewarming, the cardiopulmonary bypass was discontinued uneventfully. The postoperative course was uncomplicated.

The tumor in the right atrial cavity, which was 48 × 45 mm in size, showed necrosis, congestion, and edema (fig. 3a, b). Histologically, the tumor was composed of intersecting fascicles of abundant large spindle cells with markedly bizarre nuclei and numerous mitotic figures (10 per 10 high-power fields; fig. 3c). Necrosis and myxoid degeneration were also seen. Immunohistochemically, the tumor cells were positive for α-smooth muscle actin and desmin (fig. 3d, e), while they were negative for pancytokeratin, CD31, CD34, and myogenin. The Ki-67 labeling index was about 70% in the hot spot (fig. 3f). Together with the clinical appearance and immunological characteristics of the tumor, a diagnosis of primary leiomyosarcoma originating from the inferior vena cava was made.

The patient underwent radiotherapy (55 Gy/25 Fr), as well as chemotherapy comprising 3 courses of 60 mg/m² doxorubicin triweekly as first-line chemotherapy, which led to a partial response. Then, the patient was administered eribulin.

**Discussion**

We reported a case of leiomyosarcoma originating from the inferior vena cava and extending to the right atrium. Although complete resection of the tumor was difficult, surgical treatment was selected to avoid progression of hepatic failure, pulmonary embolization [4], and circulatory collapse. After the surgery, the patient was undergoing chemo- and radiotherapy and was followed up on an outpatient basis.

We also performed a PubMed literature search of the past 10 years by entering the search terms 'leiomyosarcoma' and 'inferior vena cava' [3, 5–120]. These terms returned 196 articles with 322 cases (table 1). As reported, women were affected about 2.5-fold more often than men, although the mean age did not differ between genders (data not shown). The most prevalent symptoms were pain and/or discomfort, most frequently in the abdomen, and only 5.8% of the patients did not have any symptoms related to the leiomyosarcoma. Thus, as has been done in our patient, ultrasonographic examination may facilitate the detection of leiomyosarcoma in the inferior vena cava in subjects with gastrointestinal symptoms or edema.

Survival depends on the tumor’s size, location, and complete surgical resection [39]; the efficacy of chemotherapy and radiotherapy is limited [109, 121]. In the current study, data regarding surgery was available for 233 patients. Those who underwent surgery (n = 217) had significantly better survival than those who did not (n = 16) (fig. 4a). When patients who were reported in the papers published between 2007 and 2012 (n = 115) were compared with those reported in the papers published between 2012 and 2016 (n = 127), the prognosis was significantly better by log-rank test (fig. 4b). The rate of surgical resection (either incomplete or complete) in the publication period between 2012 and 2016 (138/151; 91.4%) was found to be significantly higher than that in the period between 2007 and 2012 (137/162; 84.6%; p = 0.083 by χ² test). The median survival period for the publication period of 2007–2016 was 6.75 years. The 5-year survival rate has been reported to be approxi-
approximately 50% after complete en bloc resection [1, 122] in papers published in the last century; however, an improvement in prognosis in recent years is suggested by the literature review of the current study.

In a recent report, Lv et al. [117] summarized the reports on 30 vascular leiomyosarcoma cases with involvement of the heart that had been listed on PubMed for the past 20 years. Of the 30 cases, 14 had right ventricular involvement. The average age at onset was 53.6 years, and there was a female dominance (67%). The mean follow-up survival time for patients with single cardiac cavity involvement was 15 months, which seems to be much lower than without cardiac cavity involvement.

In summary, we reported on a 38-year-old female patient suffering from abdominal distension, lower extremity edema, and dyspnea and diagnosed with leiomyosarcoma of the inferior vena cava extending to the right atrium. Multimodality imaging should be considered for patients with suspected symptoms – even if they are often nonspecific – for early diagnosis and therapy.

**Statement of Ethics**

The current case report was following the Guidelines of the Ethics Committee at Osaka Medical College.

**Disclosure Statement**

The authors declare that they have no conflicts of interest.

**References**


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Fig. 1. Chest X-ray (a) and electrocardiogram (b) on admission.

Fig. 2. Clinical images. a, b Coronal (a) and transverse (b) sections of computed tomography (CT) images. A tumor is visible in the right atrium that is continuously present within the inferior vena cava (arrows). c, d Coronal (c) and transverse (d) sections of magnetic resonance images. e, f Coronal (e) and transverse (f) sections of PET/CT-merged images. Increased FDG uptake may be observed in the right atrium (arrows).
Fig. 3. Histological analysis of the tumor. a Macroscopic appearance of the tumor resected from the right atrial cavity. b Cut surface of the tumor. c Hematoxylin and eosin staining. d Staining for α-smooth muscle actin. e Staining for desmin. f Staining for Ki-67. Original magnification ×100.

Fig. 4. Kaplan-Meier curve of the survival of the patients reported on in the past 10 years. a Subcategorized according to whether surgery had been performed or not. Patients who had undergone surgery had a significantly improved prognosis when compared with their counterparts who had not been surgically treated. b Subcategorized according to the year of publication. p values were obtained with the log-rank test.
Table 1. Summary of the papers on leiomyosarcoma in the inferior vena cava published during the past 10 years

<table>
<thead>
<tr>
<th>Women/men/unknown, n</th>
<th>229/92/1</th>
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<tbody>
<tr>
<td>Mean age ± SD, years</td>
<td>54.4±13.7</td>
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Symptoms at presentation (n = 139), n (%)

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<tr>
<th>Symptom</th>
<th>n</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Pain or discomfort</td>
<td>111</td>
<td>(79.9)</td>
</tr>
<tr>
<td>Edema</td>
<td>27</td>
<td>(19.4)</td>
</tr>
<tr>
<td>Mass</td>
<td>13</td>
<td>(9.4)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>12</td>
<td>(8.6)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>9</td>
<td>(6.5)</td>
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Therapies, n (%)

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<tr>
<th>Therapies</th>
<th>n</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Chemotherapy and radiotherapy (n = 248)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy alone</td>
<td>60</td>
<td>(24.2)</td>
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<tr>
<td>Radiotherapy alone</td>
<td>48</td>
<td>(19.4)</td>
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<tr>
<td>Both chemo- and radiotherapy</td>
<td>21</td>
<td>(8.5)</td>
</tr>
<tr>
<td>Neither chemo- nor radiotherapy</td>
<td>119</td>
<td>(48.0)</td>
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Surgery (n = 313)

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<th>n</th>
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<tr>
<td>Surgical resection</td>
<td>275</td>
<td>(88)</td>
</tr>
<tr>
<td>No surgery</td>
<td>38</td>
<td>(12)</td>
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